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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,905	07/25/2003	Guido Franzoso	21459-94575	2235

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BARNES & THORNBURG
P.O. Box 2786
Chicago, IL 60690-2786

EXAMINER	
PHAM, AUDREY S	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,905	FRANZOSO ET AL.	
	Examiner	Art Unit	
	Audrey S. Pham	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-35 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-35 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Re: Franzoso *et al.*

Claims 1-35 are pending.

Note: Claim 8 is an improper dependent claim because Claim 8, which depends from Claim 6, does not further limit Claim 6 (See MPEP 608.01(n)). Alternatively, Claim 8 lacks a proper antecedent because it is unclear which limitations the term " the molecule" referenced. For the purpose of including Claim 8 in the restriction groupings, it was assumed that Claim 8 refers to "the agent" of Claim 6.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by an agent that that increases the percentage of cells that undergo apoptosis wherein the agent is selected from the group consisting of antisense, siRNA, or ribozymes, classified in class 435, subclass 6.

II. Claims 1, 2, 6, 8, drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by an agent that that increases the percentage of cells that undergo apoptosis wherein the agent is a peptide, classified in class 435, subclass 7.1.

III. Claims 1, 2, 7, drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by an agent that that increases the percentage of cells that undergo apoptosis wherein the agent is a small molecule, classified in class 435, subclass 4.

IV. Claims 1, 9-17 drawn to a method for modulating programmed cell death comprising contacting a cell with a cNDA molecule that encodes a Gadd45 protein that protects the cell from programmed cell death, classified in class 435, subclass 7.1.

V. Claims 18, 30, drawn to a method to identify agents that modulate JNK signaling, comprising determining whether the agent binds to Gadd45β and assaying for activity of the bound Gadd45β to determine the effect on JNK signaling, classified in class 435, subclass 4.

VI. Claim 19, drawn to a method for obtaining a mimetic that is sufficient to suppress JNK activation by interacting with JNKK2, comprising designing the mimetic to mimic the function of a Gadd45 protein contacting the mimetic to a system that comprises the JNK pathway and determining whether there is suppression of JNK signaling, classified in class 435, subclass 4.

VII. Claims 20-21, 24, drawn to a method for screening and identifying an agent that modulates JNK pathway *in vitro*, comprising obtaining a target component of the JNK pathway exposing a cell to the agent and determining the ability of the agent to modulate the JNK pathway, classified in class 435, subclass 325.

NOTE: Upon election of Group VII above, Applicant must further elect ONE agent from those listed in Claim 21 or Claim 24 as each agent is structurally, physically, chemically and functionally different and therefore represents a different invention. The patentability of each agent must be considered separately. Note this in not an election of species. Applicants is reminded that any claims not reading on the elected agent will be withdrawn as being drawn to a non-elected invention.

VIII. Claim 22, drawn to a method for screening and identifying an agent that modulates JNK activity *in vivo* comprising obtaining a candidate agent administering the agent to a non-human animal and determining the level of JNK activity in the animal compared to JNK activity in animals not receiving the agent, classified in class 435, subclass 4.

IX. Claim 23, drawn to a method for identifying an agent that prevents Gadd45β from blocking apoptosis comprising contacting cells that express high levels of Gadd45β comparing apoptosis and inferring from differences in apoptosis in treated versus control

cells whether the agent prevents Gadd45β from blocking apoptosis, classified in class 435, subclass 4.

X. Claim 25, drawn to a method of treating degenerative disorders and other conditions caused by effects of apoptosis in affected cells, said method comprising obtaining a molecule that interferes with the activation of JNK pathways and contacting the affected cells with the molecule, classified in class 514, subclass 1.

XI. Claims 26-27, a method of aiding the immune system to kill cancer cells by augmenting JNK signaling comprising obtaining an inhibitor to block JNK signaling and contacting the cancer cells with the inhibitor, classified in class 514, subclass 1.

XII. Claim 28, a method for transactivating a *gadd45β* promoter comprising binding NF-kB complexes to promoter elements of *gadd45β* and assaying for *gadd45β* gene expression, classified in class 435, subclass 4.

XIII. Claim 29, a method for treating cancer, comprising increasing JNK activity by inhibiting Gadd45β function and administering inhibitors that interfere with Gadd45β function, classified in 424, subclass 9.1.

XIV. Claims 31-32, drawn to a molecule with a nucleotide sequence having Gene Bank Acc. # AF441860 that functions as a *gadd45β* promoter, that is an element of the promoter at amino acid positions according to FIG 8, classified in class 536, subclass 23.1.

XV. Claim 33, drawn to a molecule comprising a region of Gadd45β characterized by the amino acid sequence from positions 60-114 of the full length of Gadd45β protein, classified in class 530, subclass 300.

XVI. Claims 34-35, drawn to a molecule comprising a binding region of JNKK2 characterized by the amino acid sequences from the sequence identified as SEQ ID NO: 50, classified in class 530, subclass 300.

The inventions are distinct, each from the other for the following reasons:

The inventions of groups XIV-XVI and the methods of groups I-XIII are related as products and processes of use. The inventions can be shown to be distinct if one or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § 806.05(h)]. In the instant case, the nucleic acid molecules or the amino acid molecules, as claimed, can be used in a materially different process such as in methods of developing binding assays, methods of purification, or methods of making said molecules.

The inventions of Groups XIV-XVI encompass multiply distinct and independent products that encompass different functional as well as structural formulas. Group XIV encompasses a molecule with a nucleotide sequence that functions as a *gadd45β* promoter. Group XV is drawn to a molecule comprising a region of Gadd45β characterized by the amino acid sequence of Gadd45β protein. Group XVI is drawn to a molecule comprising a binding region of JNKK2 characterized by the amino acid sequence identified as SEQ ID NO: 50. Any relationship between a polynucleotide of group XIV and polypeptide of group XV and XVI is dependent upon the information provided by nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, the amino acid sequence encoding a region of Gadd45β is distinct from the amino acid sequence represented by a binding region of JNKK2. Because the polynucleotide or polypeptide sequences are distinct from each other, each group would require a separate search in the literature and sequence databases. Currently, there are approximately eight different databases that accompany the results of a search of one discrete amino acid or nucleotide sequence and each result set from a particular database must be carefully considered. Therefore, a search of the inventions of all groups would impose a substantial search burden since a search for one group would not be used to determine the patentability of the other groups.

The inventions of groups I-XIII are materially distinct methods, which differ at least in objectives, method steps and reagents. For example, groups I-IV are drawn to methods with an objective different from the other groups, modulating pathways leading to programmed cell death. Group V is drawn to a method to identify agents that modulate JNK signaling. Group VI is drawn to a method for obtaining a mimetic that is sufficient to suppress JNK activation by interacting with JNKK2. Group VIII is drawn to a method for screening and identifying an agent that modulates JNK activity *in vivo*. Group IX is drawn to a method of identifying an agent that prevents Gadd45β from blocking apoptosis. Group X is drawn to a method of treating degenerative disorder and other conditions. Group XI is drawn to a

method of aiding the immune system. Group XII is drawn to a method of transactivating a gadd45β promoter. Group XIII is drawn to a method for treating cancer. Furthermore, while groups I-IV have similar objectives, each group employs different reagents and steps to modulate pathways leading to programmed cell death. For example, group I modulates by interfering with a target by an antisense agent, group II modulate by interfering with a target by a peptide agent, group III modulates by a small molecule and group IV modulates by contacting a cell with a cNDA that protects that cell from programmed cell death. Searching all of the groups with all of the different reagents, steps or objectives would invoke a high burden of search.

These inventions are distinct for the reasons given above and they have acquired separate statuses in the art as shown by their different classifications. The search required for one group is not required for the other groups and vice versa. For these reasons, restriction for examination purposes as indicated is proper.

Species Election

One or more of the above invention groups contain multiple generic claims which include a plurality of alternatively usable substances or members. These alternative limitations are independent or distinct inventions such that they do not share a common utility or share a substantial structural feature disclosed as being essential to that utility. Because they are not so closely related, a search and examination of the entire claim cannot be made without undue burden. The members of the alternative groupings are described in the following:

Group I (Claims 3-5) is generic to a plurality of disclosed patentably distinct species comprising the following agents: antisense, siRNA, and ribozyme.

Group IV (Claims 13-16) is generic to a plurality of disclosed patentably distinct species comprising the following molecules to protect programmed cell death: TNFα, Fas, TRAIL and a gentoxic agent.

Upon election of Group I or IV, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Rejoining Claims

NOTE:

The Examiner has required restriction between product and process claims. Where Applicant elects claim(s) directed to a product and the product claim(s) is/are subsequently found allowable, the withdrawn process claim(s) that depend(s) from or otherwise include all the limitations of the allowable product claim(s) will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if an amendment is presented prior to a final rejection or allowance, whichever is earlier. Amendment submitted after final rejection is governed by 37 CFR 1.116; amendment submitted after allowance is governed by 37 CFR 1.312.

In the event of a rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claim(s) and process claim(s) may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the withdrawn process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Inventorship Amendment

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended to be in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request, as set forth in 37 CFR 1.48(b), and by a processing fee, as set forth in 37 CFR 1.17(i).

Contact Information

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Audrey S. Pham whose telephone number is (571) 272-3323. The Examiner can normally be reached during the hours of 8:30 AM - 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jeffrey Siew, can be reached during business hours at the telephone number: (571) 272-0787. The fax number for the organization, where this application or proceeding is assigned, is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Audrey S. Pham
Patent Examiner
Art Unit 1642

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER